Original Article
Sevoflurane versus total intravenous anesthesia for cardiac surgery

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Abstract: Objective: To compare the effect of sevoflurane and total intravenous anesthesia (TIVA) on anesthesia induction, maintenance and postoperative recovery in patients receiving cardiac surgeries. Methods: Overall, 80 patients admitted in our hospital to receive cardiac surgery between January 2015 and January 2017 were enrolled in our study. They were randomized into the sevoflurane anesthesia (SA) group (n=40) and the total intravenous anesthesia (TIVA) group (n=40) in terms of a random number table. Between the two groups, anesthesia induction parameters including time to pain-free, loss of eyelash reflex and intubation; anesthesia maintenance parameters including cardiopulmonary bypass time, anesthesia time, operation time, intraoperative mean arterial pressure (MAP), heart rate (HR) and blood oxygen saturation (SpO_2), the total dosage of vasoactive agents (dopamine and nitroprusside) and urine volume; other postoperative outcomes including length of hospital stay, adverse reactions, complications and return of spontaneous heartbeat were compared. Results: The time to pain-free, loss of eyelash reflex and intubation in the SA group were strikingly shorter than those in the TIVA group (P=0.031, P=0.045, P=0.016). MAP before intubation and HR before intubation, immediately and 3min after intubation were observed to be lower in the SA group (P=0.023, P=0.033, P=0.025, P=0.036). The time for cardiopulmonary bypass (CPB), anesthesia and operation were significantly shorter (P=0.031, P=0.018, P=0.017), urine volume was more (P=0.009), and length of hospital stay was shorter (P=0.022) in the SA group than in the TIVA group. Besides, a lower rate of return of spontaneous heartbeat was also observed in the SA group (27.5%, 11/40) as compared with that of the TIVA group (80.0%, 32/40; P<0.001). Between the groups, no statistical differences were found in the incidences of postoperative adverse reactions and complications (P>0.05). Conclusion: Sevoflurane anesthesia requires shorter time for anesthesia induction and maintenance, and it improves the postoperative body rehabilitation in patients undergoing cardiac surgery as compared with total intravenous anesthesia.

Keywords: Sevoflurane anesthesia, total intravenous anesthesia, cardiac surgery, myocardium, postoperative recovery

Introduction

Total intravenous anesthesia (TIVA) is associated with reduced air pollution in the operation room and lower incidences of nausea and vomiting [1]. With the use of novel intravenous anesthesia including remifentanil and propofol anesthesia, and analgesic drugs, along with the development of computer-assisted target-controlled infusion, TIVA has been used more extensively. However, TIVA is expensive and may provoke significant postoperative pain. Sevoflurane, a new halogen inhaled anesthetic, has the advantages of rapid induction, quick recovery, easy adjustment of anesthesia depth, less inhibition of circulation and less irritation

of the respiratory tract [2]. In addition, sevoflurane sells at a lower price; therefore it is more widely used in the clinical settings. In the past, medical scholars compared the effects of sevoflurane inhaled anesthesia and propofol intravenous anesthesia and found that the former had more excellent controllability than the latter [3].

Currently, frequently-employed anesthesia techniques are as follows: first, total intravenous anesthesia; second, intravenous induction and inhalation maintenance; third, total inhalation anesthesia including maintenance and induction of inhalation. Although each technique has both advantages and disadvantages, all require

rapid induction of anesthesia, simple and convenient operation, easy management, faster and higher-quality recovery, cheaper price, as well as more acceptability for patients and their families. During the treatment of myocardial ischemia caused by seriously-damaged coronary artery ischemia, on-pump coronary artery surgery is a common clinical technique. Inhaled anesthetics have good anesthetic and myocardial protective effects [4]. In the present study, we compared the effects of sevoflurane and total intravenous anesthesia in cardiac surgery, and found that sevoflurane anesthesia had a more positive effect on the patients' myocardium recovery and postoperative recovery of the body, effectively shortened the patients' time to pain-free, loss of eyelash reflex, intubation and length of hospital stay; maintained their hemodynamics stable, shortened their time for cardiopulmonary bypass (CPB), anesthesia and operation, increased their urine volume, and reduced their rates of return of spontaneous heartbeat, as reported below.

Materials and methods

General data

A total of 80 patients undergoing cardiac surgery in our hospital from January 2015 to January 2017 were included in the present study which was approved by the Ethical Committee of our hospital. The inclusion criteria were all patients had normal renal and hepatic functions, had cardiac surgical indications, were informed of and signed the informed written consents. The patients were excluded if they had infection, renal and hepatic dysfunction, allergy to anesthetic agents, psychological disorders and mental diseases or failed to compliance with physicians' orders due to the lack of a clear awareness. The patients were randomized by a random number table into the sevoflurane anesthesia (SA) group (n=40) and the total intravenous anesthesia (TIVA) group (n=40). Only anesthesiologists and data recorders were aware of group randomization and the modalities of anesthesia.

Methods

All the surgeries in this study were performed by the same group of surgeons and anesthesiologists. After 8 hours of routine preoperative fasting, the patient entered the operation room

and was connected with multi-functional electrocardiogram for continuous monitoring of electrocardiogram and arterial oxygen saturation. With the patient under local anesthesia, a 20G puncture needle was inserted into the left radial artery for monitoring blood pressure. Then a 7F catheter was punctured into the patient's right internal jugular vein, followed by infusion of acetated Ringer's solution at 20 ml/kg/h. After that, a rapid-sequence induction of anesthesia underwent in the patients, including intravenous bolus infusion of midazolam at 0.05 mg/kg, etomidate at 0.3 mg/kg, sufentanil at 0.5 μg/kg, and vecuronium at 1 mg/kg. After placement of endotracheal tube and connection with the anesthesia machine, the patient received intermittent positive pressure ventilation, with the tidal volume at 6-8 ml/kg, respiratory frequency at 12 times/min, the air/oxygen ratio of 30%/70%, the positive end expiratory pressure at 4-6 cm H_2O, and the end-tidal CO_2 concentration at 35-45 mmHg. Continuous pumping of sufentanil at 0.3-0.5 μg/kg/h and dexmedetomidine at 0.5 μg/kg/h and intermittent injection of vecuronium were conducted. The end-expiratory sevoflurane concentrations of the patients in the SA group increased to 1-1.5 MAC by adjusting the sevoflurane volatile tank whereas those in the TIVA group received propofol at 5-10 mg/kg/h. The volatile tanks for all the patients in the SA group were closed within half an hour before completion of the surgery. Following that, the cerebral bispectral index (BIS) was used to monitor the depth of anesthesia, and the BIS value maintained at 40-50. Nasopharyngeal and bladder probes are used to monitor the body temperature. In addition, hemodynamic stability was maintained during the operation by using vasoactive drugs (dopamine or nitroglycerin) or by changing the body positions.

Outcome measures

Primary outcomes were as follows: first, the time to pain-free, loss of eyelash reflex and intubation, as well as the total dosage of dopamine and of nitroprusside; second, the mean arterial pressure (MAP), heart rate and arterial oxygen saturation (SpO_2) before and after induction, immediately and 3min after intubation.

Secondary primary outcomes included CPB time, anesthesia time, operation time, urine

Table 1. Comparison of general data between the two groups

Group	Case	Gender		Age (year)	BMI	NYHA functional class			
		Male	Female			I	II	III	IV
SA	40	21 (52.5)	19 (47.5)	56.7±7.6	63.2±10.4	2	24	12	2
TIVA	40	20 (50.0)	20 (50.0)	54.3±7.4	63.6±10.6	3	22	14	1
t/χ^2		2.71		1.886	1.638	1.432			
P		0.125		0.136	0.220	0.326			

Table 2. The time to pain-free, loss of eyelash reflex and intubation, the total dosage of dopamine and of nitroprusside of the two groups ($\overline{x}$±s)

Group	Case	Time to pain-free (s)	Loss of eyelash reflex (s)	Intubation (s)	Total dopamine (mg)	Total nitroprusside (mg)
SA	40	63.0±5.0	49.7±8.4	88.3±23.7	25.3±4.2	11.8±4.7
TIVA	40	76.0±4.8[*]	71.2±9.7[*]	162.4±21.6[*]	21.1±2.5	14.6±5.3
t		3.249	2.902	4.002	-1.488	0.685
P		0.031	0.045	0.016	0.211	0.531

Note: [*]P<0.05 for comparison with the TIVA group.

volume and length of hospital stay, adverse reactions, complications and return of spontaneous heartbeat.

Statistical analysis

Statistical analysis was performed with the use of the software SPSS, version 20.0. The count data including adverse reactions, complications and return of spontaneous heartbeat of the two groups were expressed as rates (%), and comparison between the two groups was conducted with the use of the χ^2 test. The measurement data including the time to pain-free, loss of eyelash reflex and intubation, the total dosage of dopamine and of nitroprusside, the CPB time, anesthesia time, operation time, urine volume and hospitalization were expressed as mean ± standard deviation ($\overline{x}$±s) and comparison between the two was made with the student's t-test. MAP, HR and SpO_2 at diverse time points were compared by repeated measures analysis of variance (ANOVA). A *P* value less than 0.05 was considered to be statistically significantly different.

Results

General data of the patients in the two groups

The general data between the two groups showed no statistically significant difference (P>0.05, **Table 1**).

Time to pain-free, loss of eyelash reflex and intubation, the total dosage of dopamine and of nitroprusside of the two groups ($\overline{x}$±s)

The patients in the SA group showed significantly shorter time to pain-free, loss of eyelash reflex and intubation than those in the TIVA group (P<0.05), but the differences in the total dosage of dopamine and of nitroprusside between the two groups were not significant (P>0.05, **Table 2**).

Changes in MAP, HR, SpO_2 at diverse time points of the patients between the two groups

In the TIVA group, MAP and HR before intubation were lower than those before induction (P<0.05), but SpO_2 before intubation was not different from that before induction (P>0.05). Moreover, no significant difference was observed in the changes in MAP, HR and SpO_2 before induction, immediately and 3min after intubation in the TIVA group (P>0.05). Similarly, the MAP, HR and SpO_2 before induction, before intubation, immediately and 3min after intubation were not significantly different in the SA group, either (P>0.05). The MAP, HR and SpO_2 before induction between the two groups had no differences (P>0.05). MAP was higher in the SA group before intubation (P<0.05), but it was not significantly different from the TIVA group immediately and 3min after intubation (P>0.05). Before intubation, immediately and

Table 3. Changes of MAP, HR and SpO_2 of the patients in the two groups at different time points ($\bar{x}\pm s$)

Group	Case	Time	MAP (mmHg)	HR (Time/min)	SpO_2 (%)
SA	40	Before Induction	11.7±1.4	112.2±21.4	98.1±0.5
		Before intubation	10.7±2.0*	109.7±18.4*	98.4±0.2
		Immediately after intubation	11.4±2.2	115.3±16.7*	99.5±0.5
		3min after intubation	11.7±2.0	112.8±19.1*	99.0±0.1
TIVA	40	Before Induction	11.1±1.7	115.7±18.3	98.4±0.6
		Before intubation	7.8±2.1#	95.3±17.5#	98.2±0.4
		Immediately after intubation	11.2±1.4	105.5±17.5	99.3±0.6
		3min after intubation	11.6±1.8	103.7±20.2	99.2±0.2
F			12.325	10.236	0.154
P			<0.05	<0.05	>0.05

Note: #P<0.05 for comparison within the same group before induction; *P<0.05 for comparison with the TIVA group.

Table 4. Comparison of the time for CPB, anesthesia, operation and hospitalization as well as urine volume between the two groups

Group	Case	CPB (min)	Anesthesia (min)	Operation (min)	Urine volume (ml)	Hospitalization (d)
SA	40	58.9±4.6	35.8±3.5	119.5±7.3	806±95	12.0±1.2
TIVA	40	72.0±5.2*	48.3±4.4*	144.4±8.1*	1211±113*	8.6±1.1*
t		3.268	3.851	3.955	4.752	-3.618
P		0.031	0.018	0.017	0.009	0.022

Note: *P<0.05 for comparison with the TIVA group.

3min after intubation, HRs were higher in the SA group than those in the TIVA group (all P<0.05), but no significant differences were found in SpO_2 between the two groups (all P>0.05, **Table 3**).

Comparison of the time for CPB, anesthesia, operation and hospitalization as well as urine volume between the two groups

As compared with the TIVA group, the SA group had shorter time for CPB, anesthesia and operation (P<0.05), significantly more urine volume (P<0.05), but shorter hospitalization time (P<0.05, **Table 4**).

Comparison of adverse reactions, and return of spontaneous heartbeat between the two groups

The rate of return of spontaneous heartbeat was higher in the SA group (80.0%, 32/40) than in the TIVA group (27.5.0%, 11/40; P<0.05). However, the total incidences of adverse events

and complications in the two groups were 22.5% (9/40), 20.0% (8/40), respectively, and the difference was not statistically significant (P>0.05, **Table 5**).

Complications of patients in the two groups

The incidence of complications was not significantly different between the SA group and the TIVA group (P>0.05, **Table 6**).

Discussion

Sevoflurane, a novel halogen inhalation anesthetic drug, is advantageous in fewer respiratory and circulatory impact, and better controllability. Characteristic of steady induction and no excitatory phases, sevoflurane has fewer impacts on the cardiovascular system [5]. Fang reported that the changes in heart rate and blood pressure at different time points were smaller in the SA groups than in the propofol TIVA group, suggesting that sevoflurane had little influence on the hemodynamics of the patients with heart operation [6]. The result was consistent with the smaller changes in MAP, HR and SpO_2 in the process of sevoflurane anesthesia induction in our present study. Besides, Fan et al. reported that the total dosage of dopamine and nitroprusside, urine volume and length of hospital stay were (21.1±7.5) mg, (14.6±5.3) mg, (1211±313) mL, (8.6±5.1) d, respectively, in the patients undergoing heart operations with sevoflurane induced anesthesia, and (25.3±8.2) mg, (11.8±4.7) mg, (806±295) mL, (11.0±6.2) d in the patients with total intravenous anesthesia, which were significantly inferior to those of the former group [7]. Moreover, the findings of Özarslan et al. also demonstrated that during the coronary artery bypass grafting, sevoflurane had an inhibitory effect on the microcirculation and the

Table 5. Comparison of adverse events and cardiac rate of return of spontaneous heartbeat between the two groups (n, %)

| Group | Case | Adverse events | | | | Rate of return of spontaneous heartbeat |
		Restlessness	Cough	Breath holding	Total incidence	
SA	40	4 (10.0)	3 (7.5)	2 (5.0)	9 (22.5)	32 (80.0)
TIVA	40	3 (7.5)	5 (12.5)	0 (0)	8 (20.0)	11 (27.5)*
χ^2					0.75	22.175
P					0.785	<0.001

Note: *P<0.05 for comparison with the TIVA group.

Table 6. Comparison of complications between the two groups (n, %)

| Group | Case | Complication | | | |
		Myocardial infarction	Atrial fibrillation	Mortality	Total incidence
SA	40	1 (2.5)	2 (5)	0 (0)	3 (7.5)
TIVA	40	2 (5)	1 (2.5)	0 (0)	3 (7.5)
χ^2					0.000
P					1.00

effect of inhalation anesthetics on microcirculation was eliminated within 24 hours after the surgery [8]. In contrast, the rapidly increased concentration of anesthetic in total intravenous anesthesia irritated the sympathetic nerves, increasing the patient's heart rate and blood pressure [9]. These results are in accord with the results of our study.

Liu's and other studies have demonstrated that sevoflurane can significantly reduce the myocardial ischemia-reperfusion injury after CPB [10]. Sivanna et al. have proven that sevoflurane exerts better myocardial protection for the patients who received the off-pump coronary artery bypass grafting surgery [11]. Zhu et al. have argued that desflurane has myocardial protection against early ischemia-reperfusion injury after CPB [12]. The possible mechanisms include first, sevoflurane decreases coronary vascular resistance, leading to increased coronary blood flow and reduced myocardial oxygen consumption; second, sevoflurane can effectively prevent or reduce the incidence of arrhythmia, providing myocardial protection and improvements in heart functions. As far as molecular mechanisms are concerned, studies have shown that the signal transduction process of sevoflurane involves the complex signals of promoters and effectors, as well as the signal transduction mediators, among which the most promising promoters are nitric oxide and reactive oxygen species [13-17].

Sevoflurane is highly lipid soluble, so it can transport mitochondrial electron to chain complexes I-nicotinamide adenine dinucleotide through cells and mitochondrial membranes, thereby inhibiting oxidoreductase, promoting the generation of reactive oxygen species and provoking electron leakage.

According to De Hert et al., in the patients undergoing coronary artery transplantation, sevoflurane is associated with significant reductions in the release of cardiac troponin, relieved ischemia-reperfusion injuries and shorter hospital stay, which is consistent with the finding in our study that the patients with sevoflurane had markedly shorter hospital stay than those with total intravenous anesthesia [18].

The Meta-analysis by Landoni et al. indicated that sevoflurane significantly improved complications and adverse effects and decreased mortality in patients with TIVA [19]. Chikada et al. have demonstrated that sevoflurane anesthesia does not cause significant adverse reactions and complications, and has good controllability [20]. Our study also showed that the patients in the SA group had significant reductions in restlessness, cough, breath holding and other complications, but myocardial infarction, atrial fibrillation, mortality and other adverse reactions were not significant different as compared with those in the TIVA group. The possible reason is that the initial cardiac morbidity and severity of the patients are directly related to the mortality.

Sevoflurane, whose blood/gas and oil/gas partition coefficients were 0.63 and 53.90, respectively, has a rapid process of induction and recovery and adjustable depth of anesthesia [21-23]. Zhang et al. found that the patients with sevoflurane had strikingly shorter time to pain-free, loss of eyelash reflex and intubation,

which was consistent with the result of our study [24].

In conclusion, sevoflurane anesthesia is more effective than total intravenous anesthesia in protecting myocardium in patients undergoing cardiac surgery and improving postoperative recovery of the patients.

Disclosure of conflict of interest

None.

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